ASHTON et al. Appl. No. 10/556.901

Appl. No. 10/556,90 Attv. Dkt.: 620-401

Amendment After Final Rejection

March 20, 2008

## AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

 (Withdrawn – Currently Amended) A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of <u>claim 34</u>formula I, or a pharmaceutically acceptable salt thereof:

wherein

X is CH;

 $R^{\pm}$  is H, cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or  $-NH_2$ ; or  $C_{1-4}$  alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or  $-NH_2$ ; or -OR, -NHR,  $-NR_2$  or -SR wherein R is  $-C_{1-4}$  alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or  $-NH_2$ ;

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 $R^{2}$  is H, CF<sub>3</sub>; or optionally substituted C<sub>5.6</sub> aryl, C<sub>3.7</sub> cycloalkyl, C<sub>6.7</sub> heterocyclyl or together with  $R^{4}$  an optionally substituted C<sub>3.4</sub> alkylene group wherein  $L^{3}$  and  $L^{4}$  are single bonds thus forming a C<sub>5.6</sub> ring fused with the aromatic ring to which  $L^{3}$  and  $L^{4}$  are attached:

 $R^{a}$ -is H; or optionally substituted  $C_{6-6}$ -aryl,  $C_{3-7}$ -cycloalkyl,  $C_{6-7}$ -heterocyclyl or together with  $R^{2}$ -an optionally substituted  $C_{3-6}$ -alkylene group wherein  $L^{2}$ -and  $L^{4}$ -are single bonds-thus-forming a  $C_{6-6}$ -ring fused with-the-aromatic ring to which  $L^{2}$ -and  $L^{4}$ -are attached:

R4 is H; or optionally substituted Css and or Csz heterocyclyl;

R<sup>6</sup>-is-selected from H or optionally substituted C<sub>1-7</sub>-alkyl, C<sub>5-6</sub>-aryl and C<sub>1-4</sub>
alkylene-C<sub>5-5</sub>-aryl;

 $L^4$ -is-optionally-substituted  $C_{6-6}$ -arylene,  $C_{1-4}$ -alkylene- $C_{5-6}$ -arylene-or— $L^6$ N( $(R^6)L^6$ -, or  $C_{1-4}$ -alkylene substituted by-either- $C_{1-7}$ -alkyl-or- $C_{5-7}$ -aryl, wherein  $L^6$ -and  $L^6$ -are independently-selected from optionally-substituted  $C_{1-4}$ -alkylene and  $C_{5-6}$ -arylene, and  $R^6$ -is-H or  $C_{1-4}$ -alkyl; and further wherein  $L^4$ -may be unsubstituted  $C_{1-4}$ -alkylene when X is-N:

L2 is a single bond; and

L³-and L⁴-are-independently-selected from a single-bond, optionally-substituted

C₁\_alkylene, \_L°XN(OH)C(=0)L¹0-and \_L°C(=0)N(OH)YL¹0-, wherein L⁰-and L⁴0 are

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independently selected from optionally substituted  $C_{1.4}$  alkylene,  $C_{\delta-\delta}$  arylene,  $C_{1.4}$ 

alkylene-C<sub>5-6</sub> arylene and a single bond, wherein Y is NH or a single bond.

2. (Withdrawn – Currently Amended) A method of treating a condition which can

be alleviated by inhibition of glyoxalase I, which method comprises administering to a

patient in need of treatment an effective amount of a compound of claim 37A method

according to claim 1 wherein R<sup>1</sup> is chosen from the group consisting of H and cyano.

3. (Withdrawn - Currently Amended) A method of treating a condition which can

be alleviated by inhibition of glyoxalase I, which method comprises administering to a

patient in need of treatment an effective amount of a compound of claim 38A method

according to claim 1 wherein R<sup>6</sup> is H or C<sub>1-7</sub> alkyl.

4. (Withdrawn - Currently Amended) A method of treating a condition which can

 $\underline{\text{be alleviated by inhibition of glyoxalase I, which method comprises administering to a}\\$ 

patient in need of treatment an effective amount of a compound of claim 39A method

according to claim 1 wherein L<sup>4</sup> is chosen from the group consisting of phenylene,

-CH(Ph)-, -CH<sub>2</sub>-phenylene- and -CH<sub>2</sub>C(=O)NH-phenylene-.

Claim 5. (Canceled)

6. (Withdrawn - Currently Amended) A method of treating a condition which can

 $\underline{\text{be}}$  alleviated by inhibition of glyoxalase I, which method comprises administering to a

patient in need of treatment an effective amount of a compound of claim 39A method

according to claim 1 wherein L3 is chosen from the group consisting of a single bond, -

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 $L^9YN(OH)C(=O)L^{10}$ -and  $-L^9C(=O)N(OH)YL^{10}$ , wherein  $L^9$  and  $L^{10}$  are independently selected from optionally substituted  $C_{1.4}$ -alkylene,  $C_{8.6}$ -arylene,  $C_{1.4}$ -alkylene- $C_{8.6}$  arylene and a single bond, and wherein Y is NH or a single bond.

- 7. (Withdrawn Currently Amended) <u>A method of treating a condition which can</u> be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 44. A method according to claim 6 wherein L<sup>3</sup> is a single bond.
- 8. (Withdrawn Currently Amended) <u>A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 45. A method according to claim 1 wherein L<sup>4</sup> is chosen from the group consisting of a single bond, L<sup>6</sup>YN(OH)C(=O)L<sup>10</sup>—and—L<sup>0</sup>C(=O)N(OH)YL<sup>10</sup>—, wherein L<sup>9</sup>—and L<sup>10</sup>—are independently selected from optionally substituted C<sub>1-4</sub> alkylene, C<sub>6-6</sub> arylene, C<sub>1-4</sub> alkylene-C<sub>6-6</sub> arylene and a single bond, and wherein Y is NH or a single bond.</u>
- 9. (Withdrawn Currently Amended) <u>A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 46A method according to claim 8 wherein L<sup>4</sup>-is selected from the group consisting of CH<sub>2</sub>N(OH)C(=O) , phenylene-CH<sub>2</sub>N(OH)C(=O) , phenylene-NHN(OH)C(=O) and -CH<sub>2</sub>C(=O)N(OH).</u>

Claim 10. (Canceled)

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11. (Withdrawn - Currently Amended) A method of treating a condition which

can be alleviated by inhibition of glyoxalase I, which method comprises administering to

a patient in need of treatment an effective amount of a compound of claim 47A method

according to claim 1 wherein one of R<sup>4</sup>, R<sup>2</sup> and R<sup>4</sup> are H.

12. (Withdrawn – Currently Amended) A method of treating a condition which

can be alleviated by inhibition of glyoxalase I, which method comprises administering to

a patient in need of treatment an effective amount of a compound of claim 48A method

according to claim 1 wherein two of R<sup>4</sup>, R<sup>2</sup> and R<sup>4</sup> are H.

Claims 13-20. (Canceled)

Claim 21. (Canceled)

Claims 22-29. (Canceled)

Claim 30. (Canceled)

31. (Previously Presented) A pharmaceutical composition comprising a

compound according to claim 34 or a pharmaceutically acceptable salt thereof together

with a pharmaceutically acceptable carrier or diluent.

Claims 32-33. (Cancelled)

34. (Currently Amended) A compound of formula I:

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or a salt, solvate or chemically protected form thereof wherein

X is CH;

R<sup>1</sup>, R<sup>2</sup> and R<sup>4</sup> are. [[is]] H<sub>2</sub>, eyano, halo, hydroxy, hydroxamic acid, sulfhydryl or— NH<sub>2</sub>; or G<sub>1-4</sub> alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or—NH<sub>2</sub>; or—OR,—NHR,—NR<sub>2</sub> or—SR wherein R is G<sub>1-4</sub> alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or—NH<sub>2</sub>;

 $R^{a}$  is H,  $CF_{a}$ ; or optionally substituted  $C_{6.6}$  aryl,  $C_{6.7}$  cycloalkyl,  $C_{6.7}$  heterocyclyl or together with  $R^{a}$  an optionally substituted  $C_{2.4}$  alkylene group wherein  $L^{a}$  and  $L^{4}$  are single bonds thus forming a  $C_{6.6}$  ring fused with the aromatic ring to which  $L^{a}$  and  $L^{4}$  are attached:

 $R^3$  is [[H; or]] optionally substituted  $C_{5:6}$  aryl,  $C_{3:7}$  cycloalkyl, or  $C_{5:7}$  heterocyclyl or together with  $R^2$  an optionally substituted  $C_{3:4}$  alkylene group wherein  $L^3$  and  $L^4$  are single bonds thus forming a  $C_{5:6}$  ring fused with the aromatic ring to which  $L^3$  and  $L^4$  are attached:

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R<sup>4</sup> is H; or optionally substituted C<sub>5.6</sub> aryl or C<sub>5.7</sub> heterocyclyl;

 $R^6$  is selected from H or optionally substituted  $C_{1\text{--}7}$  alkyl,  $C_{5\text{-}6}$  aryl and  $C_{1\text{--}4}$  alkylene- $C_{5\text{-}6}$  aryl;

 $L^1$  is optionally substituted [[C<sub>1-4</sub> alkylene,]]  $C_{5-6}$  arylene,  $C_{1-4}$  alkylene- $C_{5-6}$  arylene or  $-L^5N(R^5)L^6$ -, or  $C_{1-4}$  alkylene substituted by either  $C_{1-7}$  alkyl or  $C_{5-7}$  aryl, wherein  $L^5$  and  $L^6$  are independently selected from optionally substituted  $C_{1-4}$  alkylene and  $C_{5-6}$  arylene, and  $R^5$  is H or  $C_{1-4}$  alkyl;

L2 is a single bond; and

L3 is a single bond; and

 $L^4 \ [\text{[are]}]\underline{is} \ \text{independently selected from a single bond, optionally substituted $C_{4.4}$ alkylene, $-L^9YN(OH)C(=O)L^{10}$- and $-L^9C(=O)N(OH)YL^{10}$-, wherein $L^9$ and $L^{10}$ are independently selected from optionally substituted $C_{1.4}$ alkylene, $C_{5.6}$ arylene, $C_{1.4}$ alkylene-$C_{5.6}$ arylene and a single bond, wherein $Y$ is $NH$ or a single bond; and$ 

wherein the compound contains at least one -C(=O)N(OH)- group.

Claims 35-36. (Canceled)

- 37. (Previously Presented) A compound according to claim 34 wherein  $L^4$  is a  $L^9$ –C(=O)N(OH)- group.
  - 38. (Original) A compound according to claim 37 wherein L<sup>9</sup> is selected from C<sub>1-4</sub>

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alkylene and C<sub>5-6</sub> arylene.

 (Original) A compound according to claim 37 wherein L<sup>9</sup> is methylene or phenylene.

Claim 40. (Canceled)

Claims 41-43. (Canceled)

44. (Previously Presented) A compound according to claim 34 wherein R<sup>3</sup> is optionally substituted C<sub>5-6</sub> aryl.

45. (Original) A compound according to claim 44 wherein R<sup>3</sup> is phenyl.

46. (Previously Presented) A compound according to claim 34 wherein  $R^6$  is H or  $C_{1.7}$  alkyl.

47. (Original) A compound according to claim 46 wherein R<sup>6</sup> is H or C<sub>1-3</sub> alkyl.

48. (Previously Presented) A compound according to claim 34 wherein L<sup>1</sup> is phenylene, -CH(Ph)-, -CH<sub>2</sub>-phenylene- or -CH<sub>2</sub>C(=O)NH-phenylene-.

Claim 49. (Canceled)

Claim 50. (Canceled)